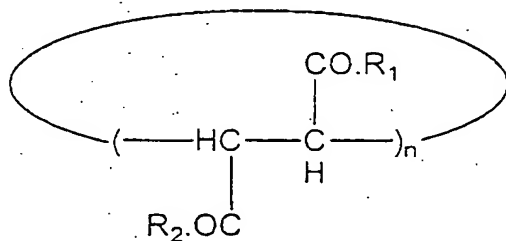


Applicant: Fumapharm AG  
Attorney's file: 54 157 V

PCT EP 03/03498

### Claims

1. A carbocyclic or oxacarbocyclic oligomer consisting of 2 to 10 units derived from fumaric acid and/or esters and/or amides thereof as repeating units.
2. A carbocyclic oligomer according to claim 1 obtained by polymerisation of the C-C double bonds of the units.
3. An oxacarbocyclic fumaric acid oligomer according to claim 1 obtained by the polarised olefinic polymerisation of the C-C double bonds and carbonyl groups and containing ether bridges in the carbocycle.
4. A carbocyclic oligomer according to claim 1, 2 or 3 wherein the fumaric acid units are derived from monomers selected from the group consisting of fumaric acid, dialkyl fumarates, monoalkyl hydrogen fumarates, fumaric acid monoamides, fumaric acid diamides, monoalkyl monoamido fumarates, and salts and mixtures thereof.
5. A carbocyclic fumaric acid oligomer according to claim 1 or 2 of the following formula (I)



wherein the radicals  $R_1$  and  $R_2$  are the same or different and are selected from the group consisting of amine radicals ( $-\text{NR}_3\text{R}_4$ ), amino acid radicals ( $-\text{NH}-\text{CH}(\text{COOH})-\text{R}_6$ ), peptide radicals having 2 to 100 amino acids, alcohol radicals ( $-\text{OR}_5$ ) and a hydroxyl radical,

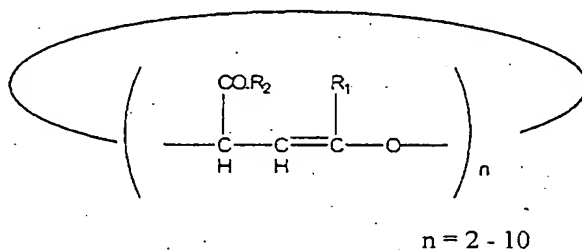
n is an integer between 2 and 10,

the radicals  $R_3$  and  $R_4$  are the same or different and are selected from the group consisting of hydrogen,  $C_{1-24}$  alkyl radicals, the phenyl radical and  $C_{6-10}$  aralkyl radicals,

the radical  $R_5$  is selected from the group consisting of hydrogen,  $C_{1-24}$  alkyl radicals, the phenyl radical and  $C_{6-10}$  aralkyl radicals,

and the radical  $R_6$  represents the side chain of a natural or synthetic amino acid.

6. An oxacarboxylic fumaric acid oligomer according to claim 1 or 3 of the following formula (IV)



wherein the radicals  $R_1$  and  $R_2$  are the same or different and are selected from the group consisting of amine radicals ( $-\text{NR}_3\text{R}_4$ ), amino acid radicals ( $-\text{NH}-\text{CH}(\text{COOH})-\text{R}_6$ ), peptide radicals having 2 to 100 amino acids, alcohol radicals ( $-\text{OR}_5$ ) and a hydroxyl radical,

n is an integer between 2 and 10,

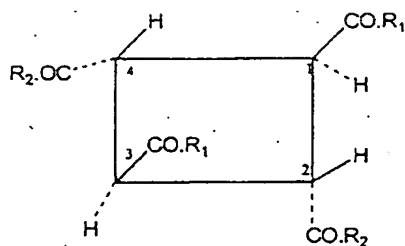
the radicals  $R_3$  and  $R_4$  are the same or different and are selected from the group consisting of hydrogen,  $C_{1-24}$  alkyl radicals, the phenyl radical and  $C_{6-10}$  aralkyl radicals,

the radical  $R_5$  is selected from the group consisting of hydrogen,  $C_{1-24}$  alkyl radicals, the phenyl radical and  $C_{6-10}$  aralkyl radicals,

and the radical  $R_6$  represents the side chain of a natural or synthetic amino acid.

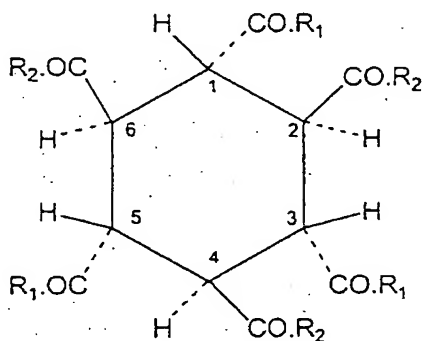
7. An oligomer according to claim 5 or 6, wherein the radicals  $R_3$ ,  $R_4$  and  $R_5$  are the same or different and are selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, t-butyl, pentyl, cyclopentyl, 2-ethyl hexyl, hexyl, cyclohexyl, heptyl, cycloheptyl, octyl, vinyl, allyl, 2-hydroxyethyl, 2- or 3-hydroxypropyl, 2,3-dihydroxypropyl, 2-methoxyethyl, methoxymethyl and 2- or 3-methoxypropyl.
8. An oligomer according to claim 5 or 6 wherein  $R_1$  represents an amine radical and  $R_2$  represents an alkoxy radical  $-OR_5$  or  $-OH$ .
9. An oligomer according to claim 5 or 6 wherein  $R_1$  and  $R_2$  each independently represent an alkoxy radical or hydroxyl radical.
10. An oligomer according to claim 9 wherein  $R_1$  and  $R_2$  are independently selected from the group consisting of methoxy, ethoxy, propoxy, isopropoxy, n-butoxy, sec-butoxy, tert-butoxy, phenoxy, and pentoxy.
11. An oligomer according to claim 9 wherein  $R_1$  and  $R_2$  are both methoxy.
12. A carbocyclic or oxacarbocyclic oligomer according to any of the previous claims containing 2 to 3 units derived from fumaric acids and/or esters and amides thereof.
13. A carbocyclic oligomer according to any of the previous claims wherein all of the carbonyl groups carrying the radicals  $R_1$  and  $R_2$  are arranged as substituents in the trans position to each adjacent substituent.

14. A carbocyclic oligomer according to claim 5 represented by the formula (II)



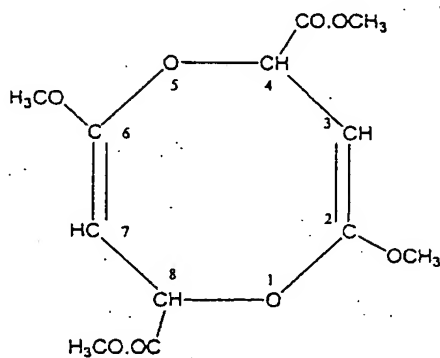
wherein  $R_1$  and  $R_2$  are as defined in claim 5.

15. A carbocyclic oligomer according to claim 5 represented by the formula (III)

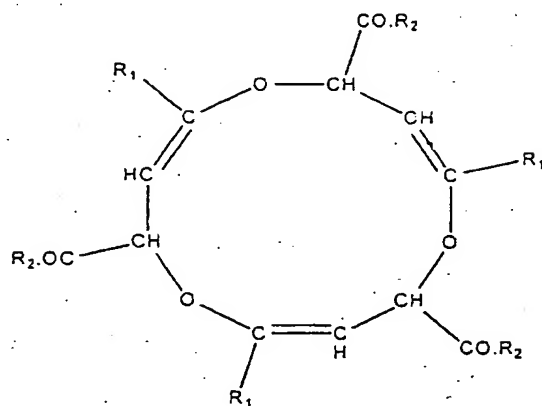


wherein  $R_1$  and  $R_2$  are as defined in claim 5.

17. An oxacarbocyclic oligomer according to claim 6 represented by the formula (V)



16. An oxacarbo-cyclic oligomer according to claim 6 represented by the formula (IV)



wherein  $R_1$  and  $R_2$  are as defined in claim 6.

18. The use of a carbocyclic or oxacarbo-cyclic oligomer according to any of the previous claims for preparing a pharmaceutical preparation.
19. The use according to claim 18, the pharmaceutical preparation being intended for treating an autoimmune disease, for transplantation medicine, for treating mitochondrial diseases and diseases that may be influenced by NFkappaB.
20. A pharmaceutical preparation containing a fumaric acid oligomer according to any of the claims 1 to 17.
21. A pharmaceutical preparation according to claim 20, said pharmaceutical preparation being available in a form suitable for oral, rectal, transdermal, dermal, ophthalmological, nasal, pulmonary or parenteral application.
22. A pharmaceutical preparation according to claim 20, said pharmaceutical preparation being present in the form of tablets, coated tablets, capsules, granulate, solutions for drinking, liposomes, nano-particles, nano-capsules, micro-capsules, micro-tablets, pellets or powders as well as granulate filled in capsules, micro-tablets filled in capsules, pellets filled in capsules, nano-particles filled in capsules or powder filled in capsules.

23. A pharmaceutical preparation according to claim 22, said pharmaceutical preparation being present in the form of nano-particles, micro-pellets or micro-tablets which, optionally, may be filled in sachets or capsules.
24. A pharmaceutical preparation according to claim 22 wherein the solid oral dosage forms are provided with an enteric coating.
25. A pharmaceutical preparation according to any of the claims 20 to 24 which contains an amount of fumaric acid oligomer corresponding to 10 to 500 mg of fumaric acid.
26. The use according to any of the claims 19 to 20 for preparing a pharmaceutical preparation
  - (1) for the therapy of an autoimmune disease selected from the group consisting of polyarthritis, multiple sclerosis, graft-versus-host reactions, juvenile-onset diabetes, Hashimoto's thyroiditis, Grave's disease (Basedow disease), systemic Lupus erythematosus (SLE), Sjogren's syndrome, pernicious anaemia and chronic active (= lupoid) hepatitis;
  - (2) for use in transplantation medicine;
  - (3) for the therapy of mitochondrial diseases selected from the group consisting of Parkinson syndrome, Alzheimer's disease, Chorea Huntington disease, retinopathia pigmentosa or forms of mitochondrial encephalomyopathy; as well as
  - (4) for the therapy of NF-kappaB mediated diseases selected from the group consisting of progressive systemic scleroderma, osteochondritis syphilitica (Wegener's disease), cutis marmorata (*livedo reticularis*), Behcet disease, panarteriitis, colitis ulcerosa, vasculitis, osteoarthritis, gout, arteriosclerosis, Reiter's disease, pulmonary granulomatosis, types of encephalitis, endotoxic shock (septic-toxic shock), sepsis, pneumonia, encephalomyelitis, anorexia nervosa, hepatitis (acute hepatitis, chronic hepatitis, toxic hepatitis, alcohol-induced hepatitis, viral hepatitis, jaundice, liver

insufficiency and cytomegaloviral hepatitis), Rennert T-lymphomatosis, mesangial nephritis, post-angioplastic restenosis, reperfusion syndrome, cytomegaloviral retinopathy, adenoviral diseases such as adenoviral colds, adenoviral pharyngoconjunctival fever and adenoviral ophthalmia, AIDS, Guillain-Barré syndrome, post-herpetic or post-zoster neuralgia, inflammatory demyelinating polyneuropathy, mononeuropathia multiplex, mucoviscidosis, Bechterew's disease, Barrett oesophagus, EBV (Epstein-Barr virus) infection, cardiac remodeling, interstitial cystitis, diabetes mellitus type II, radiosensitisation of malignant tumours, multi-resistance of malignant cells to chemotherapeutic agents (multi-pharmaceutical preparation resistance in chemotherapy), granuloma annulare and cancers such as mamma carcinoma, colon carcinoma, melanoma, primary liver cell carcinoma, adenocarcinoma, kaposi's sarcoma, prostate carcinoma, leukaemia such as acute myeloid leukaemia, multiple myeloma (plasmacytoma), Burkitt lymphoma and Castleman tumour.